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My dear Pappenheimer:

I was pleased to see your paper with Barksdale in the last number of the Journal of Bacteriology, as I have been looking forward for some time to a clarification of the issue raised by this work, especially its relationship to genetic transduction by phage as in Salmonella.

I am preparing a review on genetic exchange in bacteria and would very much appreciate documentation for the assertion that "Every lysogenic cell is a toxigenic cell", made, for example, on page 230 of your discussion. The story in diphtheria is certainly quite different from that in Salmonella, but on this crucial point I have not been able to find any explicit reference to an adequate experiment. Might I have overlooked or misinterpreted such an experiment in your paper? If so I would appreciate your enlightening me on it. What I have in mind as a test of this assertion would be a routine examination for lysogenicity of the bacterial survivors after exposure to phage, without prior selection in regard to their toxic quality. Your experiments have clearly shown that every toxigenic isolate is lysogenic, but as I read the paper, only the converted isolates were tested for lysogenicity. This is therefore a test only of the converse hypothesis, namely that every toxigenic is lysogenic.

Concerning the relationship of your story with Salmonella, I would be very surprised indeed if the role of the phage turns out to be the same in both cases. If every lysogenic isolate does prove to be toxigenic, then of course the phage could not be regarded as the passive vector of transduction. May I recall at this point the published definition of "genetic transduction", which includes "transformations" (i.e. changes) that are demonstrably the result of a transfer of genetic fragments by whatever mechanism, be it chemically extracted DNA or be it presumably similar material carried by phage. Whether lysogenization per se is transduction may prove a matter of viewpoint on the nature of phage. But clearly, before the phage could be finally and rigorously ruled out as a passive vector in your system, it would have to be shown that no lysogenized bacteria (of an appropriate strain) failed to be toxigenic. It would not be enough that phage that had been propagated on a non-toxic strain was capable of conferring toxigenicity to another non-toxic strain, so long as there were any possibility that the defects in the two strains were non-homologous. (cf. the analogy with the non-motility factors in Salmonella recently described in the Journal of General Microbiology.) The force of your argument on page 230 is somewhat stronger than appeared at

first reading, since the text does reveal that the same non-toxic strain had been used to propagate the phage and for toxic conversion.

We would be interested in some clarification of the details of the propagation of the phage on strain C7. The primary source of this phage appears to be a "lwoffate" from a toxic, lysogenic, C7. It was not obvious to us whether the subsequent "purification" of this batch of phage on C7-sensitive was sufficient to exclude any possibility of carryover of phage that had not been propagated on the new non-toxic host (i.e. what was the ratio of absolute input : output). This would be perhaps of small importance if lysogenicity were a sufficient, as well as a necessary, condition of toxigenicity; however, we have encountered a striking case of an undoubted transduction which occurs with a very high efficiency per lysogenization, approaching 50% (but strictly dependent on the genotype of the previous bacterial host).

For my review, I would therefore be indebted to you for any explicit statement of fact that I might quote on the sufficiency of lysogenicity as a condition of toxigenicity in an otherwise competent strain. I had had a brief correspondence with Neal Groman on this same subject about a year ago, but it somehow lapsed before I was able to get from him any definite assertion on this point.

May I ask that you continue to send me your papers in this field, to be exchanged, of course.

Yours sincerely,

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Associate Professor of Genetics

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